

noma of the ureter before the Urological Section of the California Medical Association, reporting a case which was diagnosed prior to surgical intervention consisting of nephro-ureterectomy, unfortunately too late, as the patient died seven months later from generalized metastases.

Early diagnosis of primary carcinoma of the ureter is a well worth while objective, as surgical removal offers the only chance of cure. In reviewing the literature in 1934, I found that Crane and Knickerbocker reported an eight-year cure, and Kraft an eleven-year cure, both by employing complete nephro-ureterectomy. Most of the patients treated by nephrectomy and subsequent ureterectomy died later from metastasis. In view of these statistics, one should always attempt to employ complete nephro-ureterectomy as the method of surgical attack for carcinoma of the ureter.

One should always think of primary carcinoma of the ureter in patients presenting general symptoms of cancer, and who present a triad of symptoms consisting of hematuria, lumbar pain, and tumefaction of the kidney, in whom ureteral obstruction is encountered, and in whom one can reasonably rule out stone, ureteral stricture and tumor of the kidney. The hematuria of primary cancer of the ureter, as of other cancers of the urological tract, is often microscopical in nature, but is usually present. Doctor Crane has covered the salient points in establishing a positive diagnosis. Unfortunately, in some patients in whom the tumor has occluded the lumen of the ureter, one is unable to pass by the obstructing growth in order to perform retrograde pyelography, and advanced destructive hydro-nephrosis will not permit secretion of opaque media injected intravenously, and in these patients the characteristic filling defect of the ureter is not to be obtained.

Additional reports of these rare cases of cancer of the ureter will keep us cancer-minded and make us be on the lookout for these obscure conditions.

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PAUL A. FERRIER, M. D. (65 North Madison Avenue, Pasadena).—Primary carcinoma of the ureter has been regarded as so rare that it is not often considered in diagnosis.

Doctor Crane mentions seventy-one proved cases. In the last four years Dr. A. G. Foord has encountered four additional cases at autopsy at the Huntington Memorial Hospital, Pasadena. These will be reported in detail later. They had not been seen by a urologist, and some of them had been diagnosed as ovarian tumors. I have operated on one further unreported case which proved to be a squamous-cell type, originating about midway in the right ureter. It had encircled the lumen, causing a complete closure. It blocked the venous return of the lower half of the ureter so that there were varicosities under the mucosa, causing profuse bleeding. The pyelographic media could not be injected beyond the carcinoma. All that could be diagnosed about the kidney was that it was not large to palpation and not tender. No intravenous dye was secreted. The pre-operative diagnosis was tumor of the ureter, possibly secondary to tumor of the kidney. This being suspected at the primary operation, a complete nephro-ureterectomy was done. The ureter was adherent to the common iliac vessels at the brim of the pelvis, and it was with some trepidation that they were freed. It was realized that carcinomatous tissue had extended beyond the ureter. The patient lived two years and died of generalized carcinoma.

In a large number of reported cases a nephrectomy has been done primarily and later a ureterectomy. While the nature of the case will often prevent a preoperative diagnosis of carcinoma of the ureter, such diagnoses have been made and substantiated, as in one case which I saw with Doctors Carl Rusche and S. K. Bacon. This was later proved at operation. In this case a filling defect in the ureter was observed, with rapidly advancing hydronephrosis.

One naturally thinks of papillary tumor of the renal pelvis with implants down the ureter, and in many cases this cannot be excluded. It is at least worth while to be prepared to do a complete nephro-ureterectomy in case of suspected tumor of the ureter.

I observed Doctor Crane's case in surgery. The dense perirenal adhesions and infiltrating growth made surgery extremely difficult.

STOMACH MUCOSAL CHANGES IN A-AVITAMINOSIS*

By ALVIN J. COX, JR., M.D.
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DISCUSSION by Garnett Cheney, San Francisco; A. G. Foord, M. D., Pasadena.

FOR a number of years there have been reports in the literature concerning lesions in the stomach in some way related to dietary deficiencies, but there has been little correlation between the type of deficiency and the type of lesion produced. Clinically, this subject has been discussed by Stepp, who pointed out that there need not necessarily be a deficiency in the diet, since destruction of the vitamin in the gastro-intestinal tract, or failure of absorption, may produce deficiency in the body.

STUDIES ON ANIMALS

Of the many observations on different kinds of animals suffering from the effects of vitamin deficiencies of various sorts, most of the studies of the stomach have been made on the rat. Here the bulk of the reported changes have occurred in the fore-stomach, or squamous epithelium-lined rumen portion, and so have no counterpart in the stomach of man. Pappenheimer and Larimore, in 1923, thought ulcers in this region were due to ingested hair. A number of authors have found gastric ulcers in rats on diets deficient in vitamin B, and a few have been convinced that vitamin A deficiency was the cause of similar lesions, though in the complete study of vitamin A deficiency by Wolbach and Howe, in 1925, no gastric lesions are mentioned. Recently, Howes and Vivier have reported evidence to indicate that some substance present in whole yeast, but not in yeast extracts, is important in preventing development of ulcers in the rat stomach. Of importance in this connection are the current reports of frequent ulcers in the gizzards of chickens fed diets deficient in a newly separated fat soluble dietary factor referred to as vitamin K.

In short, there is evidence that ulcers develop in the stomach of animals of various species more readily when the diet is not adequate, but the type of deficiency is not agreed upon by the different authors.

VITAMIN A DEFICIENCY

My relatively few experiments have been confined to the study of vitamin A deficiency, and the positive evidence derived from carefully controlled experiments indicates that deficiency of this, or some closely associated substance, in the diet of albino rats is of etiological importance in the production of ulcers, not only in the rumen portion, but in the glandular portion of the stomach toward

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The experiments reported in this communication were carried out in the Pathological Institute of the University of Freiburg, Germany. Further details, as well as microphotographs of the tissue changes, may be found in Ziegler's *Beiträge zur path. Anat. u. z. allg. Path.* 98:362, 1937.

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the pylorus and along the lesser curvature; in other words, in the parts of the stomach commonly the site of peptic ulcers in man.

EXPERIMENTAL STUDIES

White rats of two different age groups (seven and fourteen weeks) were used, and each group control and test groups of four animals were selected. Individual cages were used, and a vitamin A-free diet, prepared according to Wolbach and Howe, was administered in controlled quantities. The control diet differed from the experimental diet only in that it contained butter instead of lard as a source of fat. The older animals were killed after seven weeks on the diet, and the younger ones were allowed to live (approximately ten weeks) until they would no longer take the prescribed quantity of food. They were then killed before they had been without food more than twenty-four hours. In the first group of animals no lesions were found in any organs; but in the second, aside from the well-known epithelial changes characteristic of vitamin A deficiency, all of the experimental animals showed small ulcers in the pyloric portion of the stomach, particularly at the lesser curvature. These ulcers were tiny, not over one millimeter in diameter, had elevated margins, and microscopically, although there was a surrounding inflammatory reaction, they showed no evidence of chronicity in any portion. They were certainly acute lesions. One animal showed eight such lesions, and all ulcers found were confined to the portion of the stomach lined by mucus-secreting pyloric glands, where there was also an increase in visible intra- and extracellular mucus. The fundus mucosa showed no changes of any kind, and the rumen portion showed only small nodular proliferations of the epithelium except for several small ulcers in one animal.

COMMENT

These mucosal lesions cannot be considered specific for vitamin A deficiency, in the first place, because other things may produce ulcers in this portion of the stomach, and, secondly, since the ulcers were all very recent, perhaps occurring during the terminal period of starvation before the animals were killed. The control rats were also starved before being killed, so it is concluded that, although in themselves the ulcers are not specific, the circumstances under which they appeared were not adequate to produce ulcers in the control rats—with the exception of one very tiny erosion in the stomach of one control animal, seen only during routine serial sectioning of the stomach.

These findings in the vitamin A-free rats might be interpreted in one of two ways: as results of injury to a normal mucosa by something abnormal in the environment, such as an increased HCl content of the gastric juice, or as the effect of injury to an abnormally susceptible mucosa by substances normally present—in my experiments augmented by the terminal period of starvation.

The first possibility is made less attractive by the clinical data of Stepp, Boller, Will, and others, indicating that, in man, vitamin A deficiency is

associated with a decrease in gastric acidity, and by experimental work of Verder and Petran in monkeys which showed no change in the gastric secretion during periods of vitamin A deficiency.

Evidence of change in the cells of the stomach mucosa of my animals were demonstrable only in the mucus-secreting cells. In every case the acid-secreting portions of the mucosa were structurally normal. Only the mucus-producing pyloric glands showed evidence which might indicate increased susceptibility to injury. In addition to the ulcers, the mucosa in this area showed the increase in intra- and extracellular mucus above referred to. In considering the question of whether this increase in mucus is related directly to an increased vulnerability of the cells, one must, of course, consider the possibility that it represents merely an accumulation due to decreased digestion by the gastric juice. This, however, would not explain the accumulation within the cells. It seems more likely that an actual increase in mucus secretion existed. With special staining reactions I was unable to detect any difference in character of this mucus from that normally covering the mucosa of the rat stomach, so there is no reason to believe that the mucus was deficient in its protective action. I think it more likely that the increased mucus production is a compensatory mechanism on the part of the less-resistant mucosal cells.

Whether this change in the rat stomach has any counterpart in man is difficult to say, but it is possible that the reports by von Bergmann and others, of an increased incidence of peptic ulcer, during the spring, represents a result of decreased vitamin A intake during the winter months. A relationship between this incidence of human peptic ulcers and ulcers in the rat is suggested by the results of Siebert's observation that histamin more readily produces peptic ulcer in the rat in the spring than at other times.

IN CONCLUSION

Apart from such speculation, I believe the reported experiments have demonstrated a definite change in the glandular mucosa of the stomach of rats on a vitamin A-free diet predisposing it to injury by the gastric juice. Presumably, the exciting cause in my animals was a twenty-four-hour period of partial starvation, with failure of neutralization of the gastric juice in this period. Possibly other irritating substances might have acted similarly. As nearly as could be determined, the dietary substance protecting against these changes was vitamin A, though the possibility of some other vitamin in butter being important has not been absolutely ruled out.

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DISCUSSION

GARNETT CHENEY, M.D. (210 Post Street, San Francisco).—Any experiments attempting to correlate pathological changes in the gastric mucosa with a dietary deficiency are most welcome. Evidence is gradually accruing that such a deficiency is one important factor and, perhaps, a basic factor, in the development of certain types of gastritis and of peptic ulcer formation. Improvement in atrophic gastritis coincident with liver therapy is an established clinical fact. The seasonal variation in the incidence

of peptic ulcer may well be due to changes in diet, and a number of authors have stated that "the vital resistance" of the gastric mucosa is dependent upon an adequate vitamin intake. The nature of this vitamin is unknown to date.

In the chick experiments referred to by Doctor Cox, an erosive gastritis is an almost constant finding when the birds are fed on a diet lacking in fresh greens, but containing adequate amounts of vitamins A, B, C, and D. The gastric lesions may be prevented by the addition of certain fresh greens and cereals to the diet, or cleared up by the subsequent administration of these same substances. The antierosion substance is not vitamin K, the antihemorrhagic vitamin, but is also fat-soluble, and has its origin in the same foods as vitamin K. It has not yet been satisfactorily isolated.

It is not unlikely that the gastric lesions produced in rats may, in reality, be due to a deficiency of this unknown antierosion factor. It, as well as vitamin A, is apparently lacking in the diet used by Doctor Cox. Such an explanation of the development of these ulcers in rats would account for the confusion which has heretofore existed in this field of research. Further experiments directed toward clarifying this important subject are urgently needed.

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A. G. FOORD, M.D. (749 Fairfax Avenue, Pasadena).—Doctor Cox's paper is of interest chiefly because of the almost negative results obtained by extreme deprivation of vitamin A, even to the point of producing characteristic epithelial changes in other organs. The author shows good judgment in not overemphasizing the minute ulcers, or rather acute erosions, found in these badly diseased animals. In human beings superficial erosions of the stomach mucosa are not uncommonly found in a variety of conditions, especially following minute hemorrhages in the mucosa, interpreted usually as preagonal in origin. Possibly the ulcers in these rats are the consequence of similar small hemorrhages, or, as the other states, due to some effect apart from the specific avitaminosis. The fact that they are acute ulcers leads one to believe that vitamin deficiency plays little rôle in their formation. Were they specific, one should expect ulcers of varying ages and sizes.

THE LURE OF MEDICAL HISTORY†

STATE MEDICAL ASSOCIATION AND OTHER REMINISCENCES

By DOUGLASS W. MONTGOMERY, M.D.
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PART I*

IT is indeed a pleasure to receive this testimonial‡ from my colleagues, and it is well worth while to have lived seventy-eight years and to have practiced medicine for fifty in order to receive it.

EARLY MEETING PLACES OF THE SAN FRANCISCO COUNTY MEDICAL SOCIETY

The honor taking place in such delightful surroundings accentuates its value. We may fittingly recall in this, our annual meeting, the energy and foresight of the late Reginald Knight Smith and his comrades who secured this beautiful home for us.

Our meetings used to be held in Shields Hall on O'Farrell Street, where is now the City of Paris

† A Twenty-Five Years Ago column, made up of excerpts from the official journal of the California Medical Association of twenty-five years ago, is printed in each issue of CALIFORNIA AND WESTERN MEDICINE. The column is one of the regular features of the Miscellany department, and its page number will be found on the front cover.

* Editor's Note.—This paper will appear in two parts.

‡ For tribute to Dr. Douglass W. Montgomery, and resolution unanimously voted at the meeting of the San Francisco County Medical Society, on December 14, 1937, see CALIFORNIA AND WESTERN MEDICINE, January, 1938, p. 63.

store. We were there but for the evening; it was no home; and it was the meeting place of some secret society, I do not know which. It did not furnish, through its professional atmosphere, much medical inspiration. We had, however, many a good meeting in it.

ON BOOKS

The few books and magazines received were taken care of by Mr. Duncombe, who kept a medical bookstore on Sutter Street. Duncombe afterward established an ambulance service.

After a time, with the natural accumulation of journals, the space available by Duncombe became too narrow, and I took the library until we secured quarters in the Spring Valley Building, now the City of Paris.

I recall an amusing instance showing the temperament and the relationship of two interesting men of that time. Dr. Harry M. Sherman occupied offices with Dr. George Chismore. Sherman was a bit masterful and in some ways took charge of Chismore, who was amenable and long-suffering with the vagaries of his friend. It occurred to Sherman that Chismore had not enough genito-urinary literature for a man whose practice was rapidly tending that way, so he went to Duncombe's bookstore and ordered all available books. On their arrival he stacked them beside Chismore's bed, and Chismore dutifully read down through the pile.

AN EARLY MEDICAL OFFICE

When I came to San Francisco I rented two rooms in a two-story frame building on the northwest corner of Sutter and Mason streets. The rooms were a front and back parlor, the usual type of medical office at that time. They had none of the conveniences such as running water, etc.; they were just furnished rooms. There was a row of such residences on the south line of Geary Street between Powell and Stockton, all occupied by doctors' offices. It was called Murderers' Row, and the old surgery, with its heavy death rate, deserved the epithet.

SAN FRANCISCO DURING MY EARLY DAYS

The sidewalks were of wood. When those on Market Street were torn up, gangs of youngsters followed the workmen to pick up the coins that had dropped through the cracks during years of use.

The streets were cobbled. Recently, on visiting Mexico, I met with this kind of pavement and it gave me a homey feeling. The street-cars were horse-drawn, as were all the vehicles of the town; and the horses were, of course, accompanied by swarms of flies, which were excellent carriers for streptococci, furnishing the medical profession with lots of impetigo cases.

It was a dusty city, clouds of which blew about, and we did not have to prescribe calcium—we swallowed amounts of it.

The west wind, the horse droppings, and the sand, were an enduring plague only conquered on the arrival of the bitumen pavement; and with the sand came the fleas. To these latter many people were exquisitely sensitive, and one of my friends,